Dissecting the psychosis continuum

VALORISATION

Societal relevance

Psychotic disorders are associated with high burden for patients themselves as well as for their family members and friends, although prevalence is relatively low (0.5-1% for schizophrenia, 2.5-3.5% for psychotic disorders[1]). This is directly due to significant impairments in academic performance and occupational functioning, difficulties with interpersonal relationships and experiences of stigmatisation and discrimination, all resulting in substantially reduction in quality of life. Additionally, expenses for mental disorders and psychotic disorders in particular are among the highest of all healthcare expenses in the Netherlands[2]. The total costs for mental disorders including psychotic disorders are the combination of direct healthcare costs, non-medical costs including extra resources for social service and education, and indirect costs due to work absence or early retirement. These indirect costs may emerge from impairments, disability, premature death, and legal problems due to loss of productivity[3], and form the largest proportion of all costs for psychotic patients[4]. Overall, it can be concluded that psychotic disorders are a substantial burden for the affected individual, his/her social circle, those involved in the life and treatment of these patients and for society as a whole. Therefore, early diagnosis, intervention and preferably prevention are needed. A better understanding of the phenomenology, underlying mechanisms and psychological processes involved in the transition of subclinical symptoms towards disorder will help to reach that goal.

In order to elucidate the complex and multi-factorial aetiology of psychotic disorders and to improve prevention and intervention strategies focus of research has shifted from the population of psychotic disorder patients, especially schizophrenic patients, to first episode psychosis patients and at the lower end of the psychosis continuum to individuals with subclinical psychotic symptoms at clinical high risk for psychosis (CHR-P) as well as (non-help seeking) individuals in the general population with psychotic-like experiences. The current thesis investigated potential mechanisms and risk factors involved in the development from incidental psychotic-like experiences and subclinical psychotic symptoms to a first psychotic episode. The epidemiology and phenomenology of these experiences and associated factors was examined in both in longitudinal studies and Experiences Sampling Method (ESM) studies in daily life.

Target audience

The findings of this thesis are relevant for individuals with subclinical psychotic symptoms, psychotic patients, health care professionals and policy makers.

The results of **chapter 2** and **chapter 3** provide important information for both health care professionals as well as policy makers. Self-report measures for psychotic experiences are effective as screening instruments for the presence of potential (subclinical) psychotic symptoms, which should then be examined in detail by clinical interview. The use of a semi-structured psychosis risk assessment interview like the CAARMS or the SIPS is advised as it allows validation of an experience as a true subclinical symptom while also obtaining detailed information about the frequency of a symptoms and determination of CHR-P or psychosis status. Importantly, it has been suggested that clinical early detection teams may need to further extend their services into the community so that these individuals have better access to specialized mental health care[5]. However, in **chapter 2** it was found that (false-positive) self-reported psychotic experiences by individuals from the general population were mostly transitory in nature and only a small subsample of individuals developed true psychotic symptoms. This finding supports the recommendation that screening with self-report measures and subsequent assessment of CHR-P state should be primarily offered to selected samples of subjects who are already distressed by mental problems and seeking help for them[6]. Use for prevention in non-help-seeking subjects in the general population should be discouraged[7], as this strategy is not cost-effective due to false-positive rates.

The results of **chapter 2** highlight the importance of targeting low social functioning in early interventions as individuals who developed future psychotic symptoms were already characterised by deterioration in social functioning. Social skills training and family involvement to create a supportive environment can help to improve social functioning[8] which in turn might prevent further development of psychotic symptoms.

Chapter 2 furthermore showed high neuroticism (i.e. a tendency to show emotional instability, and react with increased anxiety, fear, and sadness[9]) is an important predictor of persistence and further development of psychotic symptoms. The results of **chapter 4** further highlight the close relationship between stress, symptoms and low mood. Increased emotional reactivity for small daily life stressors in individuals at clinical high risk for psychosis may be an important underlying mechanism in the process towards transition to psychotic disorder. Furthermore, (subclinical) psychotic symptoms can be

regarded as an additional source of distress. So both CHR-P and first episode psychosis patients are thus likely to benefit from psychoeducation and non-specific early interventions aimed at stress-reduction and enhancement of effective coping skills.

Results of **chapter 5** stress the need for thorough investigation of the exact nature of subclinical psychotic symptoms. Results tentatively suggest that severity of symptoms and risk for transition are likely to be higher for individuals reporting both feelings of suspiciousness as well as hallucinations, although this should be examined more carefully in a longitudinal study. Health care professionals need to be aware of the central role of emotion-related processes, anxiety and self-esteem for the occurrence of hallucinations and suspiciousness in daily life. Use of ESM can help bridge the gap between the professional's office and the patient's daily life. It can help to unravel symptomatic and behavioural patterns as it supplies both the individual patient and clinician with large amount of detailed, reliable and ecologically valid information about symptoms and their relationships with mood, anxiety, self-esteem all in the social context of daily life.

Innovation and implementation

Recently, studies have started to investigate the application of ESM interventions. Currently, the effectiveness of a newly developed ecological momentary intervention that targets elevated stress sensitivity, altered reward-experience, and psychological flexibility based on principles of Acceptance and Commitment Therapy (ACT) in CHR-P and first episode psychosis patients is being evaluated in the INTERACT study. The effectiveness of ACT is compared with a treatment as usual control group, of which some receive participants receive CBT specifically developed to treat (subclinical) psychotic symptoms. This ongoing ACT in daily life study extends standard ACT therapy with real life training and exercises through a dedicated device, thereby enhancing participants' ACT-based skills and techniques. Furthermore, a new study will use ESM as a monitoring and detection tool for changes in affective and psychotic symptomatology that could serve as warning signs for relapse in psychotic patients who are in symptomatic remission and want to gradually reduce and stop their anti-psychotic medication use.

The use of ESM in clinical practice and psychosis care specifically is still limited, but has great potential to improve personalized treatment as ESM is now available via mobile phone applications. Recent development and availability of web-based feedback systems offers patients and health care professionals access to real-life data on emotional en symptomatic dynamics. ESM can help to refine the diagnostic process and monitor af-

fective and psychotic symptomatology in daily life. As mood and symptoms are assessed 'in the moment' and in the context of daily life, they are not influenced by memory biases hampering traditional retrospective clinical interviews and questionnaires assessing longer time periods. ESM allows patients to accurately report changes in their emotions and behavioural pattern and reveals which emotional and/or behavioural patterns are in need of change. The implementation of ESM in clinical practice does require that professionals are trained in how gain access to, and then interpret and use ESM data in a therapeutic fashion.

As part of my activities as a psychologist at the mental healthcare institute GGzE Eindhoven, division Early Psychosis, I am involved in the implementation of ESM as a diagnostic and monitoring tool as part of regular care for first episode psychosis patients. In this fashion I can implement the knowledge of ESM that I gained during my PhD track in clinical practice. Furthermore, I am able to contribute to both of the above mentioned ESM studies as a research practitioner.

Knowledge dissemination

The present research was and will be published in peer-reviewed journals and presented at national and international research conferences. In this way, research results and methodological developments can be discussed with other scientists, what in turn stimulates development and refinement of knowledge and theories about the development of psychotic disorders. Furthermore, the results were and will be made public at more clinically oriented conferences to inform health care professionals and policy makers. By involving health care professionals in research projects, especially those focussed on the development and refinement of treatment options, valuable information can be gained on flaws of current options and feasibility of proposed solutions. By working together, scientists and health care professionals can greatly impact on the lives of patients and their families and society as a whole by developing and implementing more efficient treatment options. Finally, results were and will be made public conferences and symposia, magazines and websites managed by patient organisations that are easily accessible to the general population including patients and their families. It is the responsibility of the scientific community to actively involve patients and their families in scientific research. They can provide valuable insights on challenges they are facing, provide feedback on interventions and when relevant, on the usability of (proposed) technological tools. Adequate dissemination of knowledge will help to reduce stigmatisation in professionals, patients and the general population.

REFERENCES

1. Perala J, Suvisaari J, Saarni SI, Kuoppasalmi K, Isometsa E, Pirkola S, . . . Lonnqvist J. Lifetime prevalence of psychotic and bipolar I disorders in a general population. *Arch Gen Psychiatry.* 2007; 64:19-28.
2. Verbeek M, Knispel A, Nuijen J. *GGZ in tabellen 2013-2014.* Utrecht: Trimbos Instituut, Netherlands Institute of Mental Health and Addiction; 2015.
3. Rössler W, Joachim Salize H, van Os J, Riecher-Rössler A. Size of burden of schizophrenia and psychotic disorders. *Eur Neuropsychopharmacol.* 2005; 15:399-409.
4. Gustavsson A, Svensson M, Jacobi F, Allgulander C, Alonso J, Beghi E, . . . Olesen J. Cost of disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol.* 2011; 21:718-779.
5. Mills JG, Fusar-Poli P, Morgan C, Azis M, McGuire P. People meeting ultra high risk for psychosis criteria in the community. *World Psychiatry.* 2017; 16:322-323.
6. Fusar-Poli P. Why ultra high risk criteria for psychosis prediction do not work well outside clinical samples and what to do about it. *World Psychiatry.* 2017; 16:212-213.
7. Fusar-Poli P, Cappucciati M, Rutigliano G, Schultze-Lutter F, Bonoldi I, Borgwardt S, . . . McGuire P. At risk or not at risk? A meta-analysis of the prognostic accuracy of psychometric interviews for psychosis prediction. *World Psychiatry.* 2015; 14:322-332.
8. Thompson E, Millman ZB, Okuzawa N, Mittal V, DeVylder J, Skadberg T, . . . Schiffman J. Evidence-based early interventions for individuals at clinical high risk for psychosis: a review of treatment components. *J Nerv Ment Dis.* 2015; 203:342-351.
9. McCrae RR, Costa Jr PT, Martin TA. The NEO-PI-3: a more readable revised NEO Personality Inventory. *J Pers Assess.* 2005; 84:261-270.